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By FAX and COURIER

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4 September 2000

Dear Sirs

International Patent Application No. PCT/US99/09346
CHIRON CORPORATION
Our Ref: N.78459 DMG/PT/sw

In response to the written opinion dated 3 August 2000, please amend this application by replacing claims pages 1420 and 1421 presently on file by new retyped pages 1420 and 1421 attached.

Three further copies of the retyped pages follow with the courier copy of this letter. To assist the Examiner I attach a copy of the original version of pages 1420 to 1421 showing in manuscript the changes made to them. A further copy of the hand-amended pages also follows with the courier copy of this letter.

Amendments

Claim 4 has been amended to refer to fragments of 14 or more consecutive amino acids. Basis for this amendment can be found at page 6 line 6 of the description.

The term "specifically" has been inserted into claim 5. Basis for this amendment can be found at page 32 line 5 of the description.

Claim 8 has been amended to refer to fragments comprising 40 or more consecutive nucleotides. Basis for this amendment can be found at page 6 line 26 of the description.

The claim dependencies of claims 9 to 15 have been corrected as indicated by the Examiner in "re item VII" of the written opinion.

Novelty
Claim 5

New claim 5 is directed towards an antibody which binds specifically to a protein according to any one of claims 1 to 3. The skilled man would interpret "an antibody which binds specifically to a protein" as meaning an antibody that binds with a high affinity to a protein of the invention but which does not bind, or binds with a much lower affinity to any other protein". If, as anticipated by the Examiner, an antibody disclosed in document D1 cross-reacts with the protein of SEQ ID NO: 1202 this antibody would fall outside the scope of new claim 5. Such an antibody to the Tbp protein of D2 will not bind specifically to the protein of SEQ ID NO: 1202 because it will bind with a higher affinity to the Tbp protein of D2. New claim 5 is, therefore, novel over D1.

Claim 8

New claim 8 encompasses fragments comprising 40 or more consecutive nucleotides. The fragment of SEQ ID NO: 1201 (positions 429 to 441) exemplified by the Examiner as being homologous to the sequence claimed in D2 (positions 496 to 508) is 12 amino acids in length. A nucleotide fragment of 40 nucleotides encodes 13 amino acids. Therefore, new claim 8 is novel over D2.

Inventive Step

New claim 4 is directed to a protein comprising a fragment which comprises 14 or more consecutive amino acids and new claim 8 is directed to a nucleic acid molecule which comprises 40 or more consecutive nucleic acids. It is submitted that a fragments of SEQ ID NO: 1202 or SEQ ID NO: 1201 of this length are inventive over the prior art document D2 because the skilled person would not have been able to derive such sequences from D2 in an obvious manner.

The protein disclosed in D2 is only 23.5% identical to the protein with the amino acid sequence shown in SEQ ID NO: 1202. The amino acid sequence disclosed in D2 is only homologous to SEQ ID NO: 1202 over small sections of the total sequence (for example, a stretch of 6 amino acids at positions 3 to 8 of SEQ ID NO: 1202 is homologous to positions 20 to 25 of the D2 sequence). It would be impossible for the skilled man to predict the sequence of a fragment of 14 amino acids of SEQ ID NO: 1202 from the disclosure of D2 simply by making conservative changes or additions to the sequence shown in D2.

The amino acid sequence of a protein fragment for use as an antigen is critical for generating antibodies specific for the native protein from which the fragment is derived. Therefore, the skilled man reading D2 would not have been able to derive protein fragments of 14 or more amino acids from SEQ ID NO: 1202 that are useful in generating specific antibodies to the *Nisseria meningitidis* protein comprising the sequence of SEQ ID NO: 1202. Similarly, the

skilled man would not have been able to derive a nucleotide fragment of more than 40 nucleotides of SEQ ID NO: 1201 from the sequence data in D2.

Please acknowledge safe receipt of this letter and enclosures by stamping and returning the attached acknowledgement copy.

Yours faithfully,

D.M. GOLDIN

CLAIMS

1. A protein comprising a fragment of an amino acid sequence from SEQ ID NO: 2790 wherein said fragment comprises at least 7 amino acids from said sequence.

2. A protein comprising an amino acid sequence selected from the group consisting of even numbered SEQ IDs from SEQ ID NO: 2 through to SEQ ID NO: 3020.

3. A protein having 50% or greater homology to a protein according to claim 1.

4. A protein comprising a fragment of an amino acid sequence selected from the group consisting of even numbered SEQ IDs from SEQ ID NO: 2 through SEQ ID NO: 3020, wherein said fragment comprises 14 or more consecutive amino acids from said sequence.

5. An antibody which binds specifically to a protein according to any one of claims 1 to 3.

6. A nucleic acid molecule which encodes a protein according to any one of claims 1 to 3.

7. A nucleic acid molecule according to claim 5, comprising a nucleotide sequence selected from the group consisting of odd numbered SEQ IDs from SEQ ID NO: 1 through to SEQ ID NO: 3019.

8. A nucleic acid molecule comprising a fragment of a nucleotide sequence selected from the group consisting of odd numbered SEQ IDs from SEQ ID NO: 1 through SEQ ID NO: 3019, wherein said fragment comprises 40 or more consecutive nucleotides from said sequence.

9. A nucleic acid molecule comprising a nucleotide sequence complementary to a nucleic acid molecule according to claim 6.

10. A nucleic acid molecule comprising a nucleotide sequence complementary to a nucleic acid molecule according to claim 7.

11. A nucleic acid molecule comprising a nucleotide sequence

complementary to a nucleic acid molecule according to claim 8.

12. A composition comprising a protein, a nucleic acid molecule, or an antibody according to any preceding claim.

13. A composition according to claim 12 being a vaccine composition or a diagnostic composition.

14. A composition according to claim 12 for use as a pharmaceutical.

15. The use of a composition according to claim 12 in the manufacture of a medicament for the treatment or prevention of infection due to Neisserial bacteria.

16. A composition comprising a protein of claim 1 wherein said composition is immunogenic.

17. A composition comprising a protein of claim 2 wherein said composition is immunogenic.

18. A composition comprising a protein of claim 3 wherein said composition is immunogenic.